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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,064	12/04/2001	Michael Campbell	MBHB00-1257-B	9564

27716 7590 06/21/2004

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 06/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,064	CAMPBELL ET AL.	
	Examiner	Art Unit	
	Deepak R Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-13,28-36,38,39,41-47 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-13,28-36,38,39,41 and 63* is/are rejected.

7)☒ Claim(s) *42-47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on April 8, 2004.

Claims 1, 3-4, 6-13, 28-36, 38-39, 41-47 and 63 are pending in this application.

Election/Restrictions

As indicated in the previous office action, the search and examination was based on the structural formula I having the variables as defined (see page 3 of paper no. 02102004) and a prior art rejection was made. The examined subgenus is provided below for convenience:

X^1, X^2 and X^3 are N; ... ... (as defined for elected species)

A is a covalent bond; ... ... (as defined for elected species)

R^1 and R^2 are H; ... ... (as defined for elected species)

(i.e., $N(R^2)(AR^1)$ together is NH_2);

Z is S; ... ... (as defined for elected species)

R^4 is optionally substituted alkyl;

m is 0; ... ... (as defined for elected species)

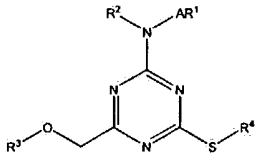
n is 0 **(i.e., T is absent)**;

p is 1; ... ... (as defined for elected species)

Y^2 is $-CH_2-$; ... ... (as defined for elected species)

and R^3 is as defined in the claims.

As applicant amended the claims to overcome the rejection, as per the guidelines of MPEP § 803.02, the search and examination of the Markush-type claims was expanded to the compounds of presently recited formula I:



wherein:

A is a covalent bond;

R^1 and R^2 are H;

(i.e., $N(R^2)(AR^1)$ together is NH_2); and

R^3 and R^4 are as defined in the claims;

and art was found. As per the guidelines, all other generic subject matter is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4, 6-13 and 28-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating atherosclerosis, does not reasonably provide enablement for treating all other disease states; diseases; or conditions encompassed by the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The scope of the claims is not adequately enabled solely based on the activity related to increasing ABCA-1 expression; raising serum levels of HDL cholesterol; or promoting cholesterol efflux, provided in the specification. First, the instant claims cover disorders that are known to exist and those that may be discovered in the future, for which there is no enablement provided. Regarding the diseases intended by the instant claims, the specification provides that "such diseases include, but are not limited to, diseases of artery, in particular coronary artery diseases" (see page 4). There is no disclosure of what other diseases are intended or contemplated by the instantly recited activity. The specification explains that the term 'coronary artery disease' as a "chronic disease in which there is a 'hardening' of the coronary arteries" (see page 14). The only specific disease provided in the specification is atherosclerosis. High levels of LDLs are associated with atherosclerosis and HDLs help to remove cholesterol from the blood. In humans, the development of atherosclerosis is positively and inversely correlated with the plasma levels of low density lipoproteins (LDL) and high density lipoproteins (HDL)

respectively. Therefore, elevated HDL levels and lower LDL levels are preferred in a therapeutic approach for atherosclerosis.

'Coronary artery diseases' are generally due to subintimal deposition of atheromas in the large and medium-sized arteries serving the heart and the complications include angina pectoris, unstable angina, cardiac arrhythmias, myocardial infarction, etc. and the specification does not provide any nexus between the disclosed activity and all the diseases encompassed by the instant claims, especially those of the coronary artery.

Test procedures and assays are provided in the specification in Examples 17-21 and it is concluded that the compounds of the invention 'increased ABCA-1 gene expression' or 'stimulated cholesterol efflux', however, there is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of the various diseases embraced by the instant claims. The disorders encompassed by the instant claims include e.g., coronary artery diseases, some of which have been proven to be extremely difficult to treat, as the precise pathogenesis of all of the coronary artery diseases is unknown or unclear. There are multitude of risk factors contributing to various coronary artery diseases. The treatment for a specific coronary heart disease varies depending on the symptoms and how much the disease has progressed. Not one compound -- let alone a genus of thousands of compounds, could possibly be effective against all types of coronary heart diseases generally.

Further, there is no reasonable basis for assuming that the compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent (based on the definitions of R^1, R^2, R^3 and R^4) and there is no

basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

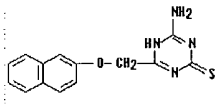
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Hataba, CAPLUS Abstract No. 128:3618 (1997). The instant claims read on reference disclosed compound of RN 198837-20-6 (the structural formula depicted below for convenience), which is

tautomeric form of the compound of structural formula I wherein $-N(AR^1)(R^2)$ is $-NH_2$; R^3 is naphthyl; and R^4 is H.

RN 198837-20-6 CAPLUS
CN 1,3,5-Triazine-2(1H)-thione, 4-amino-6-[(2-naphthalenyloxy)methyl]- (9CI)



Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36, 38-39, 41 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hataba, CAPLUS Abstract No. 128:3618. The reference teaches 1,3,5-triazinyl compound having antimicrobial activity. Claim 36 reads on reference disclosed compound, see the rejection under 35 USC 102(b) above. The remaining claims 38, 39 and 41 are drawn to

compounds wherein R^4 is alkyl, e.g., methyl, in place of the hydrogen (from the mercapto or –SH group) of the reference disclosed compound. Therefore, the instant claim is drawn to a compound which is a homolog (i.e., differing by a $-CH_2$ group) of the reference compound. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally homologous compounds would be expected to possess similar utilities. It has been held that compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. *In re Haas*, 60 USPQ 544 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950).

Allowable Subject Matter

Claims 42-47 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims limited to the examined subgenus (see page 3).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-

0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

June 16, 2004